Add B1

WHAT IS CLAIMED IS:

1. An assay for phenotyping the *patched* status of a cell, comprising detecting, in a sample of mammalian cells, the presence or absence of a genetic lesion characterized by at least one of (i) aberrant modification or mutation of a *patched* gene, and (ii) mis-expression of said *patched* gene.

2. The assay of claim 1, wherein detecting said lesion includes:

i. providing a diagonistic probe comprising a nucleic acid including a region of nucleotide sequence which hybridizes to a sense or antisense sequence of said *patched* gene, or naturally occuring mutants thereof, or 5' or 3' flanking sequences naturally associated with said gene;

ii. combining said probe with nucleic acid from said cell sample; and

iii. detecting, by hybridization of said probe to said cellular nucleic acid, the existence of at least one of a deletion of one or more nucleotides from said *patched* gene, an addition of one or more nucleotides to said *patched* gene, a substitution of one or more nucleotides of said *patched* gene, a gross chromosomal rearrangement of all or a portion of said *patched* gene, a gross alteration in the level of an mRNA transcript of said *patched* gene, or a non-wild type splicing pattern of an mRNA transcript of said *patched* gene.

3. The assay of claim 2, wherein hybridization of said probe further comprises subjecting the probe and cellular nucleic acid to a polymerase chain reaction (PCR) and detecting abnormalities in an amplified product.

4. The assay of claim 2, wherein said probe hybridizes under stringent conditions to a nucleic acid designated by SEQ ID No. 9 or 18.

5. The assay of claim 2, wherein said probe hybridizes under stringent co[illegible] to a nucleic acid designated by SEQ ID No. 18.

6. The assay of claim 2, wherein said probe further comprises a [illegible] attached to said nucleic acid and able to be detected.

7. The assay of claim 1, wherein detecting said lesio[illegible]certaining, from a methylation pattern of said *patched* gene, [illegible] absence of aberrant methylation of said *patched* gene.

8. The assay of claim 7, wherein the [illegible] sample with one or more determined by combining nucl[illegible] determining the restriction digest methylation-sensitive restric[illegible] pattern of at least a porti[illegible]

9. The assay of claim 1, wherein detecting said lesion comprises detecting the presence or absence of a non-wild type level of a *patched* protein product of said *patched* gene in cells of said cell sample.

10. The assay of claim 9, wherein the level of said *patched* protein is detected in an immunoassay.

11. The assay claim 1, wherein detecting said lesion comprises ascertaining, relative to a wild-type level of *hedgehog*-dependent *patched* signal transduction, the ability of cells in said cell sample to respond to *hedgehog* induction.

12. The assay of claim 1, wherein said cell sample is obtained from a human patient.

13. A method for diagnosing a genetic predisposition of an animal for at least one of a developmental abnormality or a proliferative disorder marked by abberant expression or activity of a *patched* gene or gene product, the method comprising detecting the presence of a predisposing mutation in a *patched* gene in cells of said animal, wherein the presence of said predisposing mutation indicates that said individual has a genetic predisposition for at least one of developmental abnormalities or a proliferative disorder.

14. The method of claim 13, wherein said genetic predisposition is basal cell nevus syndrome.

15. The method of claim 13, wherein said genetic predisposition is a predisposition for developing a carcinoma

16. The method of claim 13, wherein said genetic predisposition is a predisposition for developing a meningiomas.

17. The method of claim 13, wherein said genetic predisposition is a predisposition for developing a medullomas

18. The method of claim 13, wherein said genetic predisposition is a predisposition for developing a fibroma.

19. The method of claim 13, wherein said detecting step comprises analyzing a nucleic acid sample obtained from said animal.

20. The method of claim 13, wherein said detecting step comprises functional analysis of *patched* protein function.

21. The method of claim 13, wherein said detecting step comprises detecting antibody binding to abnormal *patched* protein.

22. A method for characterizing the phenotype of a tumor, comprising detecting the presence of an oncogenic *patched* mutation in cells of the tumor, wherein the presence

of said oncogenic mutation indicates that said tumor has a patched-associated phenotype.

23 ~~20~~. The method of claim 19, wherein said tumor is a carcinoma.

24 ~~21~~. The method of claim 20, wherein said carcinoma is a basal cell carcinoma.

25 5 ~~22~~. The method of claim 19, wherein said tumor is a meningioma.

26 ~~23~~. The method of claim 19, wherein said tumor is a medulloma

27 ~~24~~. The method of claim 19, wherein said tumor is a fibroma.

28 ~~25~~. The method of claim 19, wherein said oncogenic *patched* mutation are detected by analyzing DNA of said tumor.

29 10 ~~26~~. The method of claim 19, wherein said oncogenic *patched* mutation are detected by mRNA of said tumor.

~~30~~ ~~27~~. The method of claim 19, wherein said detecting step comprises functional analysis of patched protein function.

31 ~~28~~. The method of claim 19, wherein said detecting step comprises detecting antibody 15 binding to abnormal patched protein.

~~32~~ ~~29~~. A genetically engineered mammalian cell predisposed to develop a proliferative phenotype as a result of transfection of said mammalian cell with at least one nucleic acid construct which inhibits expression of an endogenous *patched* gene or alters the signal transduction activity of a wild-type *patched* protein.

~~33~~ ~~30~~. The cell of claim ~~26~~ 29, wherein the cell develops a carcinoma phenotype.

34 ~~31~~. The cell of claim ~~30~~ 33, wherein the cell develops a basal cell carcinoma phenotype.

35 ~~32~~. The cell of claim ~~26~~ 29, wherein the cell develops a meningioma phenotype.

36 ~~33~~. The cell of claim ~~26~~ 29, wherein the cell develops a medulloma phenotype.

37 ~~34~~. The cell of claim ~~26~~ 29, wherein the cell develops a fibroma phenotype.

~~38~~ 29 ~~35~~. A method for treating an animal having a disorder characterized by loss-of-function of a *patched* gene, comprising transfecting cells of the animal with an expression construct encoding a *patched* protein.

39 ~~36~~. The method of claim ~~35~~ 38, wherein the cells are transfected *in vivo*.

40 ~~37~~. The method of claim ~~35~~ 38, wherein the cells are transfected *in vitro*.

41 30 ~~38~~. The method of claim ~~35~~ 38, wherein the expression construct is a viral vector.

42 ~~39~~. The method of claim ~~35~~ 38, wherein the transfected cells include epithelial cells.

40. The method of claim 35, wherein the transfected cells include neuronal cells.

41. The method of claim 35, wherein the transfected cells include carcinoma cells.

42. The method of claim 41, wherein the carcinoma cells are basal cell carcinoma cells.

43. The method of claim 35, wherein the transfected cells include meningioma cells.

43. The method of claim 35, wherein the transfected cells include medulloma cells.

44. The method of claim 35, wherein the transfected cells include fibroma cells.

45. A method for treating an animal having a disorder characterized by loss-of-function of a *patched* gene, comprising administering to the animal an agent which inhibits derepression of one or more *patched*-dependent genes.